	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 06:29:25 ON 10 APR 2002

STRUCTURE FILE UPDATES: 8 APR 2002 HIGHEST RN 404822-50-0
DICTIONARY FILE UPDATES: 8 APR 2002 HIGHEST RN 404822-50-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

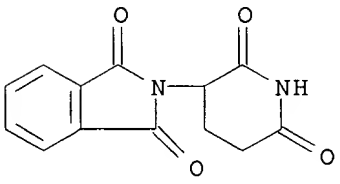
Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

```
=> s 50-35-1/rn
L1            1 50-35-1/RN

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   50-35-1  REGISTRY
CN   1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
CN   Phthalimide, N-(2,6-dioxo-3-piperidyl)- (6CI, 7CI, 8CI)
OTHER NAMES:
CN   (.+-.)-Thalidomide
CN   .alpha.-(N-Phthalimido)glutarimide
CN   .alpha.-N-Phthalylglutaramide
CN   .alpha.-Phthalimidoglutarimide
CN   1,3-Dioxo-2-(2,6-dioxopiperidin-3-yl)isoindoline
CN   3-Phthalimidoglutarimide
CN   Celgene
CN   Contergan
CN   Distaval
CN   K 17
CN   Kevadon
CN   N-(2,6-Dioxo-3-piperidyl)phthalimide
```

CN N-Phthaloylglutamimide
CN Quetimid
CN Sedoval
CN Softenil
CN Softenon
CN Talimol
CN Thalidomide
CN Thalomid
FS 3D CONCORD
DR 14088-68-7, 731-40-8
MF C13 H10 N2 O4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, HODOC*, HSDB*, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

790 REFERENCES IN FILE CA (1967 TO DATE)
44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
797 REFERENCES IN FILE CAPLUS (1967 TO DATE)
15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.96	2.17

FILE 'CAPLUS' ENTERED AT 06:30:03 ON 10 APR 2002

FILE COVERS 1907 - 10 Apr 2002 VOL 136 ISS 15

AN 2000:48781 CAPLUS
DN 132:175214
TI New anti-angiogenesis agents: review of the clinical experience with carboxyamido-triazole (CAI), thalidomide, TNP-470, and interleukin-12
AU Masiero, Laura; Figg, William D.; Kohn, Elise C.
CS Laboratory of Pathology, National Institutes of Health, Bethesda, MD, 20892, USA
SO Angiogenesis (1997), 1(1), 23-35
CODEN: AGIOFT; ISSN: 0969-6970
PB Kluwer Academic Publishers
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review with 83 refs. is given focussing on 4 agents under investigation in the US: carboxyamido-triazole (CAI), thalidomide, TNP-470, and interleukin (IL)-12. Angiogenesis was postulated to be a crit. prognostic factor and therapeutic focus for malignancy more than 2 decades ago. Recent studies indicate quant. assessments of microvessel count to be an independent prognostic variable for disease-free and overall survival in a wide variety of tumors, and that angiogenesis may be a feasible target against which to intervene pharmacol. Several new and old agents were found to have anti-angiogenic activity and have reached clin. trial. This review will focus on 4 agents under investigation in the US: carboxyamido-triazole (CAI), thalidomide, TNP-470, and interleukin (IL)-12. CAI, originally identified for its anti-invasive capacity, was shown to inhibit tumor and endothelial cell proliferation by inhibition of Ca uptake. It is administered orally, is generally well tolerated, and was shown to induce disease stabilization and occasional redns. in tumor mass. Thalidomide was shown to inhibit growth factor-induced neo-vessel formation, a process that can also explain its earlier devastating clin. toxicity. It is administered orally, and is currently in phase II clin. trials for prostate cancer, glioblastoma multiforme, and **breast cancer**. TNP-470 is a fumagillin analog that was shown in in vivo models to be a potent inhibitor of angiogenesis at concns. that are cytostatic to endothelial cells and tumor cells. Lastly, IL-12 may exert its anti-angiogenic effects through activation of interferon-.gamma. to up-regulate interferon-inducible protein-10, an anti-angiogenic cytokine. Phase I clin. trials of IL-12 have shown disease stabilization in several tumor types in response to s.c. administration or using genetically engineered IL-12-expressing patient fibroblasts. These promising new agents join the matrix metalloproteinase inhibitors as important new drugs in the anti-cancer armamentarium.
ST review angiogenesis inhibitor antitumor
IT Angiogenesis
Angiogenesis inhibitors
(new anti-angiogenesis agents)
IT Interleukin 12

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new anti-angiogenesis agents)

IT **50-35-1**, Thalidomide 99519-84-3, 1H-1,2,3-Triazole-4-carboxamide, 5-amino-1-[[3,5-dichloro-4-(4-chlorobenzoyl)phenyl]methyl]- 129298-91-5, TNP-470
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new anti-angiogenesis agents)

RE.CNT 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
TI Effects of **thalidomide** on **liver cancer** angiogenesis in mice
AN 2001:669172 CAPLUS
DN 136:379553
TI Effects of **thalidomide** on **liver cancer** angiogenesis in mice
AU Wang, Xi'an; Xiao, Zhengda; Jin, Guanqiu; Wang, Luowei; Shen, Binhong; Ding, Aini; Lu, Jiao; Shen, Min
CS Department of Gastroenterology, No.411 Hospital of PLA, Shanghai, 200081, Peop. Rep. China
SO Dier Junyi Daxue Xuebao (2001), 22(6), 561-563
CODEN: DJXUE5; ISSN: 0258-879X
PB Dier Junyi Daxue Xuebao Bianjibu
DT Journal
LA Chinese
AB The vascular suppressive effect of **thalidomide** on mice **liver cancer** angiogenesis and its mechanism were studied. The exptl. animal model with **liver cancer** was made by s.c. inoculation of mice **liver cancer** HAC cells strain in Kunming mice. Mice with **liver cancer** were divided into 4 groups: neg. control group (distd. water perfusion stomach), pos. control group (cyclophosphamide 100 mg kg-1, i.p., 1, 3, and 5 d after inoculation), **thalidomide** A group, and **thalidomide** B group. Mice in **thalidomide** A and **thalidomide** B groups were treated with **thalidomide** (50 mg kg d-1) for 1 and 5 days, resp. after inoculation. The microvessel d. (MVD), PCNA, and VEGF were detected by Envision System immunohistochem. MVD were 2.9.+-.1.3 and 10.5.+-.2.7, and pos. rate of VEGF was (0.8.+-.0.2)% and (2.2.+-.1.1)%, resp. in **thalidomide** A and B groups. Both the MVD and the VEGF were significantly lower than those in neg. control group ($P < 0.05$). The cancer suppressive rate of **thalidomide** A and B groups was 50.1% and 41.5%, resp. The results showed that **thalidomide** can inhibit the growth of mice HAC **liver cancer** through its antiangiogenic function.
TI Effects of **thalidomide** on **liver cancer** angiogenesis in mice
AB The vascular suppressive effect of **thalidomide** on mice **liver cancer** angiogenesis and its mechanism were studied. The exptl. animal model with **liver cancer** was made by s.c. inoculation of mice **liver cancer** HAC cells strain in Kunming mice. Mice with **liver cancer** were divided into 4 groups: neg. control group (distd. water perfusion stomach), pos. control group (cyclophosphamide 100 mg kg-1, i.p., 1, 3, and 5 d after inoculation), **thalidomide** A group, and **thalidomide** B group. Mice in **thalidomide** A and **thalidomide** B groups were treated with **thalidomide** (50 mg kg d-1) for 1 and 5 days, resp. after inoculation. The microvessel d. (MVD), PCNA, and VEGF were detected by Envision System immunohistochem. MVD were 2.9.+-.1.3 and 10.5.+-.2.7, and pos. rate of VEGF was (0.8.+-.0.2)% and (2.2.+-.1.1)%, resp. in **thalidomide** A and B groups. Both the MVD and the VEGF were significantly lower than those in neg. control group ($P < 0.05$). The cancer suppressive rate of **thalidomide** A and B groups was 50.1% and 41.5%, resp. The results showed that **thalidomide** can inhibit the growth of mice HAC **liver cancer** through its antiangiogenic function.
ST **thalidomide liver cancer** angiogenesis
IT Angiogenesis inhibitors
(effects of **thalidomide** on **liver cancer** angiogenesis in mice)
IT Liver, neoplasm
(hepatoma, inhibitors; effects of **thalidomide** on **liver cancer** angiogenesis in mice)

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
TI Nonsurgical treatment of **hepatocellular carcinoma**
AN 2001:818154 CAPLUS
DN 136:112075
TI Nonsurgical treatment of **hepatocellular carcinoma**
AU Aguayo, Alvaro; Patt, Yehuda Z.
CS Division of Medicine, Departments of Medical Oncology and Gastrointestinal Medical Oncology, M.D. Anderson Cancer Center, The University of Texas, Houston, TX, 77030, USA
SO Seminars in Oncology (2001), 28(5), 503-513
CODEN: SOLGAV; ISSN: 0093-7754
PB W. B. Saunders Co.
DT Journal; General Review
LA English
AB A review. While surgical resection and tumor ablation are the preferred therapies for **hepatocellular carcinoma** (HCC), these are available or appropriate in only a minority of patients. This reflects the usual comorbidity of severe underlying liver disease that either precludes surgery or makes the surgical approach extremely dangerous. Nonetheless, regional control of HCC is highly relevant and many regional strategies have been explored, including hepatic intra-arterial chemotherapy, transarterial chemoembolization, lipiodol chemoembolization, radiation therapy, cryosurgery, percutaneous ethanol injection, and radiofrequency ablation. In addn., a variety of systemic chemotherapeutic agents have been tested in HCC, including various combinations of 5-fluorouracil, doxorubicin, epirubicin, etoposide, cisplatin, and mitoxantrone, as well as interferon, tamoxifen, capecitabine, **thalidomide**, and octreotide, Published data regarding these regional and systemic therapies will be discussed in this review.
RE.CNT 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Nonsurgical treatment of **hepatocellular carcinoma**
AB A review. While surgical resection and tumor ablation are the preferred therapies for **hepatocellular carcinoma** (HCC), these are available or appropriate in only a minority of patients. This reflects the usual comorbidity of severe underlying liver disease that either precludes surgery or makes the surgical approach extremely dangerous. Nonetheless, regional control of HCC is highly relevant and many regional strategies have been explored, including hepatic intra-arterial chemotherapy, transarterial chemoembolization, lipiodol chemoembolization, radiation therapy, cryosurgery, percutaneous ethanol injection, and radiofrequency ablation. In addn., a variety of systemic chemotherapeutic agents have been tested in HCC, including various combinations of 5-fluorouracil, doxorubicin, epirubicin, etoposide, cisplatin, and mitoxantrone, as well as interferon, tamoxifen, capecitabine, **thalidomide**, and octreotide, Published data regarding these regional and systemic therapies will be discussed in this review.
ST review antitumor **hepatocellular carcinoma**
IT Temperature effects, biological
(cold, cryosurgery; nonsurgical treatment of **hepatocellular carcinoma** in humans)
IT Embolism
(embolization, chemo-; nonsurgical treatment of **hepatocellular carcinoma** in humans)
IT Temperature effects, biological
(heat, thermotherapy; nonsurgical treatment of **hepatocellular carcinoma** in humans)
IT Liver, neoplasm
(hepatoma, inhibitors; nonsurgical treatment of **hepatocellular carcinoma** in humans)
IT Antitumor agents

(hepatoma; nonsurgical treatment of **hepatocellular carcinoma** in humans)

IT Chemotherapy
Human
Radiotherapy
(nonsurgical treatment of **hepatocellular carcinoma** in humans)

IT 64-17-5, Ethanol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonsurgical treatment of **hepatocellular carcinoma** in humans)

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
TI Pharmaceutical compositions containing **thalidomide** for the treatment of **hepatocellular carcinoma**
AN 2001:643415 CAPLUS
DN 135:185507
TI Pharmaceutical compositions containing **thalidomide** for the treatment of **hepatocellular carcinoma**
IN Huang, Chun-Ying; Whang-Peng, Jia-Kang; Chen, Li-Tzong; Liu, Tsang-Wu; Chang, Jang-Yang; Hsu, Ming-Chu
PA TTY Biopharm Company Limited, Taiwan
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001018445	A1	20010830	US 2001-768442	20010124
	EP 1226824	A1	20020731	EP 2001-300601	20010124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2001240542	A2	20010904	JP 2001-23900	20010131
PRAI	TW 2000-89101826	A	20000202		

AB A pharmaceutical compn. for the treatment of **hepatocellular carcinoma** comprises **thalidomide** and a pharmaceutically acceptable carrier. Capsules each contg. 50 mg drug prepd. from **thalidomide** 50, lactose 50, corn starch 18, and Avicel 65 mg. The components were blended, passed through a No. 45 mesh-sieve, and filled into hard gelatin capsules.
TI Pharmaceutical compositions containing **thalidomide** for the treatment of **hepatocellular carcinoma**
AB A pharmaceutical compn. for the treatment of **hepatocellular carcinoma** comprises **thalidomide** and a pharmaceutically acceptable carrier. Capsules each contg. 50 mg drug prepd. from **thalidomide** 50, lactose 50, corn starch 18, and Avicel 65 mg. The components were blended, passed through a No. 45 mesh-sieve, and filled into hard gelatin capsules.
ST **thalidomide hepatocellular carcinoma** inhibitor pharmaceutical
IT Embolism
(embolization, chemo-; pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)
IT Liver, neoplasm
(hepatoma, metastasis, inhibitors; pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)
IT Antitumor agents
(hepatoma, metastasis; pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)
IT Liver, neoplasm

(hepatoma, metastatic; pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)

IT Liver, neoplasm
(hepatoma; pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)

IT Angiogenesis inhibitors
Gene therapy
Immunotherapy
(pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)

IT Hormones, animal, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)

IT 50-35-1, **Thalidomide**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. **thalidomide** for treatment of **hepatocellular carcinoma**)

=>

IT Antitumor agents
(hepatoma; effects of **thalidomide** on **liver cancer** angiogenesis in mice)
IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effects of **thalidomide** on **liver cancer** angiogenesis in mice)
IT 50-35-1, **Thalidomide**
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of **thalidomide** on **liver cancer** angiogenesis in mice)

=>

AN 2000:48781 CAPLUS
DN 132:175214
TI New anti-angiogenesis agents: review of the clinical experience with carboxyamido-triazole (CAI), thalidomide, TNP-470, and interleukin-12
AU Masiero, Laura; Figg, William D.; Kohn, Elise C.
CS Laboratory of Pathology, National Institutes of Health, Bethesda, MD, 20892, USA
SO Angiogenesis (1997), 1(1), 23-35
CODEN: AGIOFT; ISSN: 0969-6970
PB Kluwer Academic Publishers
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review with 83 refs. is given focussing on 4 agents under investigation in the US: carboxyamido-triazole (CAI), thalidomide, TNP-470, and interleukin (IL)-12. Angiogenesis was postulated to be a crit. prognostic factor and therapeutic focus for malignancy more than 2 decades ago. Recent studies indicate quant. assessments of microvessel count to be an independent prognostic variable for disease-free and overall survival in a wide variety of tumors, and that angiogenesis may be a feasible target against which to intervene pharmacol. Several new and old agents were found to have anti-angiogenic activity and have reached clin. trial. This review will focus on 4 agents under investigation in the US: carboxyamido-triazole (CAI), thalidomide, TNP-470, and interleukin (IL)-12. CAI, originally identified for its anti-invasive capacity, was shown to inhibit tumor and endothelial cell proliferation by inhibition of Ca uptake. It is administered orally, is generally well tolerated, and was shown to induce disease stabilization and occasional redns. in tumor mass. Thalidomide was shown to inhibit growth factor-induced neo-vessel formation, a process that can also explain its earlier devastating clin. toxicity. It is administered orally, and is currently in phase II clin. trials for prostate cancer, glioblastoma multiforme, and **breast cancer**. TNP-470 is a fumagillin analog that was shown in in vivo models to be a potent inhibitor of angiogenesis at concns. that are cytostatic to endothelial cells and tumor cells. Lastly, IL-12 may exert its anti-angiogenic effects through activation of interferon-.gamma. to up-regulate interferon-inducible protein-10, an anti-angiogenic cytokine. Phase I clin. trials of IL-12 have shown disease stabilization in several tumor types in response to s.c. administration or using genetically engineered IL-12-expressing patient fibroblasts. These promising new agents join the matrix metalloproteinase inhibitors as important new drugs in the anti-cancer armamentarium.
ST review angiogenesis inhibitor antitumor
IT Angiogenesis
Angiogenesis inhibitors
(new anti-angiogenesis agents)
IT Interleukin 12

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new anti-angiogenesis agents)

IT **50-35-1**, Thalidomide 99519-84-3, 1H-1,2,3-Triazole-4-carboxamide, 5-amino-1-[[3,5-dichloro-4-(4-chlorobenzoyl)phenyl]methyl]- 129298-91-5, TNP-470
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new anti-angiogenesis agents)

RE.CNT 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Alessandro, R; In Vivo 1996, V10, P153 CAPLUS
(2) Angiolillo, A; J Exp Med 1995, V182, P155 CAPLUS
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